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10/664,725	09/18/2003	Manabu Nakatani	01-1395	4358

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EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
06/11/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO.e-Office.rdg@boehringer-ingelheim.com

Office Action Summary	Application No.	Applicant(s)	
	10/664,725	NAKATANI ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 6-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' new arguments presented in the Appeal Brief regarding the lack of clear delineation in the placement of the components in the bilayered tablet of Gaviraghi are persuasive. Therefore the finality of the previous Office Action is hereby withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2 and 6-12 are rejected under 35 U.S.C. 103(a) as being obvious over Hauel et al. (AU 9210707) in view of Berstein et al. (US PGPub No. 20030220297) and Doi et al. (US PGPub No 2004/0058914 - previously cited).

Hauel et al. teach a collection of benzamidazole compounds as active agents where telmisartan is explicitly envisioned (see first listed compound in claim 6). They go on to teach tablet formulations that include one of the envisioned active agents. In particular the exemplified tablet contains 100 mg of active agent, 50 mg of lysine (a known basic amino acid), 86 mg of lactose (water soluble diluent), 1.2 mg of magnesium stearate (lubricant), 50 mg of corn starch (water soluble diluent) and 2.8 mg of polyvinylpyrrolidone (see example V; instant claims 1, -2, 7, and 9-12). When telmisartan is employed as the active agent, this composition includes a basic agent to telmisartan ratio of 1.76 to 1, a weight percentage of water soluble diluent of 29% and 1% polyvinylpyrrolidone (see instant claim 1). Hauel et al. generally teach the inclusion of conventional inert carriers and diluents that include glucose, lactose, polyvinylpyrrolidone, corn starch, and magnesium stearate in their compositions. As one of a set of explicitly envisioned carriers/diluents, it would have been obvious to one of ordinary skill in the art at the time of the invention to use either glucose or lactose in example V as functionally equivalent carbohydrate carriers/diluents (see page 53 paragraph 1; instant claim 8). Hauel et al. do not explicitly teach a poloxamer (polyoxamer) as an envisioned conventional inert carrier/diluent.

Berstein et al. teach pharmaceutical compositions that are envisioned to include telmisartan (see paragraph 224). Tablet preparations of these composition are taught to

include conventional inactive (inert) ingredients that include povidone, poloxamer 188, magnesium stearate, and lactose (see paragraph 285).

Doi et al. teach that both polyvinylpyrrolidone (povidone) and Pluronic® F68, also known as poloxamer 188, were known as binders in solid pharmaceutical dosage forms at the time of the invention (see paragraph 448; instant claims 1 and 6).

As a known conventional inert ingredient taught to have the same function as a conventional inert carrier/diluent particularly envisioned by Hauel et al., it would have been obvious to one of ordinary skill in the art to substitute poloxamer 188 for the polyvinylpyrrolidone taught in example V of Hauel et al. Given that both Hauel et al. and Berstein et al. teach many of the same conventional inert ingredients in tablet preparations where telmisartan is an envisioned active agent, there would have been a reasonable expectation of success for this substitution. Therefore claims 1-2 and 6-12 are obvious over Hauel et al. in view of Berstein et al. and Doi et al.

Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauel et al. in view of Berstein et al. and Doi et al. as applied to claims 1-2 and 6-12 above, and further in view of Palomo (US Patent No. 5,232,706) and Wienen et al. (Cardiovascular Drug Reviews 2000 18:127-154).

Hauel et al. in view of Berstein et al. and Doi et al. make obvious the pharmaceutical composition of instant claim 1 where lysine is the basic agent. This modified reference does not explicitly teach the presence of arginine.

Palomo teach lysine and arginine for use as basic compounds in a pharmaceutical formulation (see column 2 lines 38-43; instant claim 3). Wienen et al. teach that telmisartan is more soluble in a basic environment, thus the inclusion of a basic compound in the preparation improves its solubility (see page 128 paragraph 4).

It would have been obvious to one of ordinary skill in the art at the time of the invention to exchange arginine for the lysine in the composition of Hauel et al. in view of Berstein et al. and Doi et al. as a functionally equivalent basic amino acids. Therefore claims 1 and 3 are obvious over Hauel et al. in view of Berstein et al., Doi et al., Palomo, and the Weinen et al.

Claims 1 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauel et al. in view of Berstein et al. and Doi et al. as applied to claims 1-2 and 6-12 above, and further in view of Gaviraghi (previously cited).

Hauel et al. in view of Berstein et al. and Doi et al. make obvious the pharmaceutical composition of instant claim 1. In addition, the modified reference teaches the inclusion of additional active agents in the composition that include hydrochlorothiazide (HCTZ), a diuretic (see page 53 paragraph 2). Hauel et al. in view of Berstein et al. and Doi et al. do not explicitly teach a bilayered configuration for the actives or a particular matrix for the HCTZ.

Gaviraghi teach a bilayered tablet configuration that includes telmisartan in one layer and another drug in the second layer (see page 13 lines 1-2). It is further taught

that the telmisartan layer is formulated as taught in EP 0502314, which is also published as Hauel et al. (see page 11 lines 21-22).

Ohkouchi et al. teach disintegrating solid dosage forms (see abstract). In particular, HCTZ is an envisioned active for these compositions (see column 5 line 36).

As a known arrangement for telmisartan and another active within a single dosage form, it would have been obvious to one of ordinary skill in the art at the time of the invention to configure the tablet of Hauel et al. in view of Berstein et al. and Doi et al. as a bilayered tablet with telmisartan and HCTZ in the separate layers. This would also allow one of ordinary skill in the art to separately control the rate of release for each of the drugs. Given the teachings of Ohkouchi et al. regarding matrices known for the delivery of HCTZ, it also would have been obvious to utilize their matrix for the HCTZ layer in the bilayered tablet of Hauel et al. in view of Berstein et al., Doi et al., and Gaviraghi. Therefore claims 1 and 13 are obvious over Hauel et al. in view of Berstein et al., Doi et al., Gaviraghi, and Ohkouchi et al.

Claims 1 and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ambuhl et al. (US PGPub No. 2004/0198645; note international filing date is incorrect on face of PGPub, actually filed May 8, 2002) in view of Hauel et al., Berstein et al., and Weinen et al.

Ambuhl et al. teach the preparation of solid pharmaceutical dosage forms, such as tablets, where the drug is poorly water soluble (see paragraph 8). They go on to teach that the drug is included along with a surfactant or polymer and carrier where the

polymer is envisioned as polyvinylpyrrolidone, the surfactant is envisioned as poloxamer 188, and the carrier is envisioned as lactose (see paragraphs 15, 44, 74-83, and 151). A lubricant, such as magnesium stearate, is also envisioned in the composition (see paragraphs 1121-122). One method embodiment is performed by spraying a solution of the drug with surfactant onto a fluidized bed of carrier (granulation) that is then dried (see paragraph 152; instant claim 14). Ambuhl et al. also teach that these preparations have carrier composing 10% to 40% of the composition (see paragraph 88). Surfactant is present from 10% to 70% (see paragraph 56). In addition, Ambuhl et al. teach in another embodiment that the composition may be prepared by spray-drying a combination of the drug with surfactant in an aqueous solution (see paragraph 151 and 171-173; instant claim 15). An outer tablet matrix can also be present and is taught to include lactose, implying that the drug particles are combined with this outer phase material to produce a tablet (see paragraph 186; instant claim 15). This outer matrix material can comprise 20% to 60% of the composition (see paragraph 184). Ambuhl et al. do not explicitly teach the presence of a basic agent in the composition or telmisartan as the poorly water soluble drug.

Wienen et al. teach that telmisartan is poorly soluble in water, but is more soluble in a basic environment (see page 128 paragraph 4).

Hauel et al. teach a collection of benzamidazole compounds as active agents where telmisartan is explicitly envisioned (see first listed compound in claim 6). They go on to teach tablet formulations that include one of the envisioned active agents. In particular the exemplified tablet contains 100 mg of active agent, 50 mg of lysine (a

known basic amino acid), 86 mg of lactose (water soluble diluent), 1.2 mg of magnesium stearate (lubricant), 50 mg of corn starch (water soluble diluent) and 2.8 mg of polyvinylpyrrolidone (see example V; instant claims 1, -2, 7, and 9-12). When telmisartan is employed as the active agent, this composition includes a basic agent to telmisartan ratio of 1.76 to 1, a weight percentage of water soluble diluent of 29% and 1% polyvinylpyrrolidone (see instant claim 1).

Berstein et al. teach pharmaceutical compositions that are envisioned to include telmisartan (see paragraph 224). Tablet preparations of these composition are taught to include conventional inactive (inert) ingredients that include povidone, poloxamer 188, magnesium stearate, and lactose (see paragraph 285).

Since telmisartan was a poorly water soluble drug known at the time of the invention, it would have been obvious to use it in the methods taught by Ambuhl et al. The composition in example V taught by Hauel et al. falls within the set taught by Ambuhl et al. Although Ambuhl et al. do not explicitly envision the presence of the basic agent lysine, given the ability of base to solubilize telmisartan and the use of a solution of drug in their methods or preparation, it would have been obvious to include this basic agent in the drug/surfactant or drug/polymer mixture to improve the solubility of the drug. Poloxamer 188 and polyvinylpyrrolidone are taught as exchangeable entities in the compositions of Ambuhl et al. and were both known conventional inert ingredients in telmisartan preparations, as taught by Hauel et al.; thus exchange of poloxamer 188 for polyvinylpyrrolidone in the composition of example V from Hauel et al., when used in the methods of Ambuhl et al. would also have been obvious. These obvious modifications

yield the methods of clams 14 and 15; therefore claims 1, 14, and 15, are obvious over Ambuhl et al. in view of Hauel et al., Berstein et al., and Weinen et al.

Response to Arguments

Applicant's arguments filed March 15, 2010 have been fully considered but they are moot in light of the new grounds of rejection.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner, Art Unit 1615

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